Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION

1790 BROADWAY AT 58TH STREET, NEW YORK, N. Y.

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Vol. XIII **December, 1944** **No. 12**

HYPERTENSION AS VIEWED FROM ITS SURGICAL TREATMENT

PART I

The surgical treatment of hypertension is a comparatively recent addition to our medical armamentarium. Aside from unilateral nephrectomy, which almost always fails to modify the hypertensive state, and the removal of adrenal tumors, medullary or cortical, (rare causes of hypertension) surgery has consisted largely in removing portions of the sympathetic nervous system, particularly those having to do with the vasomotor control of the vascular supply of the viscera of the splanchnic bed. The purpose is to lower blood pressure by decreasing the tone of arteriolar smooth muscle. Surgical technique has varied according to the author, Adson[1], Craig[2], Peet[3], Crile[4], Smithwick[5], and Grimson[6]. The difference lies largely in the extent of these operations. This has varied from partial to total or near total denervation of the splanchnic bed; to total or near total sympathectomy. In general, it seems as if the more extensive operations have been more effective, although time may show that increasing the operation beyond a certain point may yield diminishing returns which may not compensate for an increase in untoward symptoms resulting from the attendant physiological changes.

It has been demonstrated, beyond a doubt, that in a significant percentage of patients with continued diastolic hypertension persistent lowering of blood pressure has resulted from surgical intervention of this sort. This has been associated with favorable changes in the eyegrounds, electrocardiograms, and cardiac and renal function as measured by ordinary tests as well as symptoms. It seems reasonable to conclude that the sympathetic nervous system plays a role in the mediation of increased peripheral resistance to blood flow in many hypertensive patients. This may be regarded as a modern concept. Recent data bearing upon the clinical aspects of the surgical treatment have been published and will not be discussed further in this communication.

Other concepts have emphasized vascular disease and humoral pressor substances as important factors in the causation of hypertension in man. The surgical approach to hypertension has offered the first opportunity to obtain direct information concerning the state of the arterioles, particularly those in the renal area, in living hypertensive patients. The kidneys have been inspected and biopsies for microscopic study taken at the time of lumbodorsal splanchnicectomy. Previously, the only methods of evaluating vascular disease directly, were the gross and microscopic study of autopsy material, which had disclosed that the kidneys of hypertensive patients show comparatively more evidence of damage than do other organs and tissues. This has led many to believe that renal arteriolar disease therefore antedated and in some way was the real cause of most cases of chronic hypertension in man. Others, undoubtedly the minority, have felt that this was not necessarily the fact. The finding of severely damaged kidneys at death did not prove that this condition must have existed prior to the onset of hypertension. The biopsy material introduces data pertaining to the earlier stages of hypertension in man and favors the viewpoint that renal vascular disease does not necessarily antedate the hypertensive state.

It is interesting to review some of the evidence, chronologically, which bears upon the cause of hypertension since Bright first called attention to this matter in 1827.[7] Bright observed that at death contracted kidneys were associated with hypertrophied hearts. He[8] stated that "the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately, or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant subdivisions of the vascular system." Thus, in this earliest concept, the cause was thought to be pre-existing renal disease and the effective mediator a circulating humoral substance.

This concept had as one of its most ardent supporters Johnson[9], who stated in 1872 that the most common causes of contracted kidneys "were excess of food and stimulants, with or without decided gouty symptoms, but he had seen many cases in which the disease had been a result of chronic dyspepsia in persons of strictly temperate habits. The proximate cause of the renal degeneration was the excretion of abnormal products by the gland-cells." Once the kidneys had thus been rendered cachectic, the following events transpired,[10] "in consequence of the degeneration of the kidney the blood is morbidly changed. It contains urinary excreta, and it is deficient of some of its own normal constituents. It is, therefore more or less unsuited to nourish the tissues, more or less noxious to them. The minute arteries throughout the body resist the passage of this abnormal blood. The left ventricle, therefore, makes an increased effort to drive on the blood. The result of

ANNOUNCEMENT

Plans are being made to hold the Annual Scientific Session of this Association just before the next Annual Session of the American Medical Association. Later announcements will indicate the exact time and place of such meetings. The Chairman of our Program Committee is Dr. Arlie R. Barnes, Mayo Clinic, Rochester, Minnesota, and those who wish to present papers at the Scientific Session of the American Heart Association should communicate with him as soon as possible.

this antagonism of forces is that the muscular walls of the arteries and those of the left ventricle of the heart become simultaneously and to an equal degree hypertrophied. The persistent overaction of the muscular tissues, both cardiac and arterial, is registered after death in a conspicuous and unmistakable hypertrophy".

This concept was given great impetus by the brilliant experiments of Goldblatt during the past ten years, many times confirmed by others, who demonstrated that if the blood flow through the kidneys of dogs is significantly reduced by partial clamping of the renal arteries persistent hypertension invariably resulted. Previously, Cash[10] had been able to produce experimental hypertension by excising a considerable amount of renal tissue, a more difficult and less satisfactory experimental method. Subsequently, Page[11] was able to produce chronic renal hypertension due to a constricting perinephritis, which resulted from wrapping cellophane or silk about the kidneys. Referring to his observations Goldblatt[12] in 1940 stated, "the investigations to be described here were begun because it was thought that the problem of the possible renal origin of the type of hypertension that is associated with vascular disease of the kidney, with or without accompanying renal excretory insufficiency, should be capable of solution by experiments on animals. By postulating that if the vascular disease of the kidney be responsible for initiating the hypertension, it must precede the development of the hypertension, it became necessary in some way to reproduce the vascular disease in the kidney, or to develop some method whereby the probable functional disturbances of renal circulation caused by the vascular disease could be reproduced. The effect of such vascular disease, it was assumed would be renal ischemia, and it was thought, therefore, that a solution to the problem should be possible, if a method for the production of renal ischemia in animals could be developed. . . . It appears to be established beyond reasonable doubt that the hypertension which develops after constriction of the main renal arteries, or as a result of renal ischemia produced by any method, is due to some humoral mechanism of renal origin. Evidence is accumulating to justify the conclusion that the results of these studies on animals may be directly applicable to the pathogenesis of both the benign and malignant phases of essential hypertension in man, which is associated with the presence of intrarenal or extrarenal vascular or other disease that can produce renal ischemia. Further knowledge of the pathogenesis and perhaps the treatment of this condition will depend upon the establishment of this conclusion."

The concept that primary renal arteriolar disease was the cause of hypertension was further supported by Moritz and Oldt[13], who studied the vascular changes in various organs and tissues of 100 normotensive individuals dying of various causes and 100 hypertensive patients dying of various complications of their disorder. Their study "disclosed only one situation in which the presence of arteriolar sclerosis was almost invariably associated with hypertension and where the absence of arteriolar sclerosis almost invariably betokened an absence of high blood pressure. This was in the kidneys". They felt that their findings "supported the conclusion that renal arteriolar sclerosis is the most common cause of chronic hypertension. This conclusion is in accord with the recent demonstration by Goldblatt that chronic hypertension is regularly produced in dogs and monkeys by reducing the blood flow through the kidneys (renal ischemia). The effect of the renal arteriolar sclerosis in human hypertension appears to be the functional analogue of the renal arterial clamp in experimental hypertension."

The renal humoral concept had received further support when Tigerstedt and Bergman[14] identified a substance, renin, by observing the pressor action of crude kidney extracts. Since that time, particularly during the past ten years, a vast amount of work has been carried out by many investigators in an attempt to isolate the pressor substance which is thought by many to be responsible for experimental hypertension of the Goldblatt variety and for human hypertension as well. Particularly active, have been workers in Houssay's laboratory in Argentina and Page's laboratory in this country. The evidence which has so far accumulated has recently been reviewed in detail by Landis[15] who notes "the failure of almost all observers to detect pressor activity when the blood from hypertensive animals and man or extractives of such blood have been injected in many different assay preparations". In spite of a large amount of indirect evidence favoring the humoral concept, direct proof of a pressor substance being the sole mediator of chronic hypertension in man does not as yet exist. According to Landis, failure to demonstrate a pressor substance might be "that hypertensive, as soon as it is formed, immediately leaves the circulating blood to be attached at once to the smooth muscle of the blood vessels, and in so doing produces its constrictor effect."

The concept that hypertension resulted from a primary kidney disease was first seriously contested by Gull and Sutton[16] who made a detailed study of gross and microscopic changes in various organs and tissues of patients dying of chronic Bright's disease. As a result, they concluded "this theory does not appear to us supported by the facts." Among the facts they mention are, "(1) there is a diseased state characterized by hyaline-fibroid formation in the arterioles and capillaries. (2) The kidneys may be but little if at all affected, whilst the morbid change is far advanced in other organs. (3) The contraction and atrophy of the kidney are but a part and parcel of the general morbid change. (4) It is probable that this morbid change commonly begins in the kidney, but there is evidence of its also beginning primarily in other organs. (5) In the present state of our knowledge we cannot refer the vascular changes to an antecedent change in the blood due to defective renal excretion. (6) The kidneys may undergo extreme degenerative changes without being attended by the cardio-vascular and other lesions characteristic of the condition known as chronic Bright's disease."[11]

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